An Introduction to the NIH Clinical Trials Policies

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NIH NATIONAL CANCER INSTITUTE

NCI/CRCHD Professional Development Workshop
June 3, 2019

TODAY'S FOCUS

1
PURPOSE FOR THE NEW NIH CLINICAL TRIAL REFORMS

2
INTRODUCTION TO THE NIH CLINICAL TRIAL POLICIES

3
RESOURCES TO HELP NAVIGATE THE NIH POLICIES CHANGES

Why the changes?

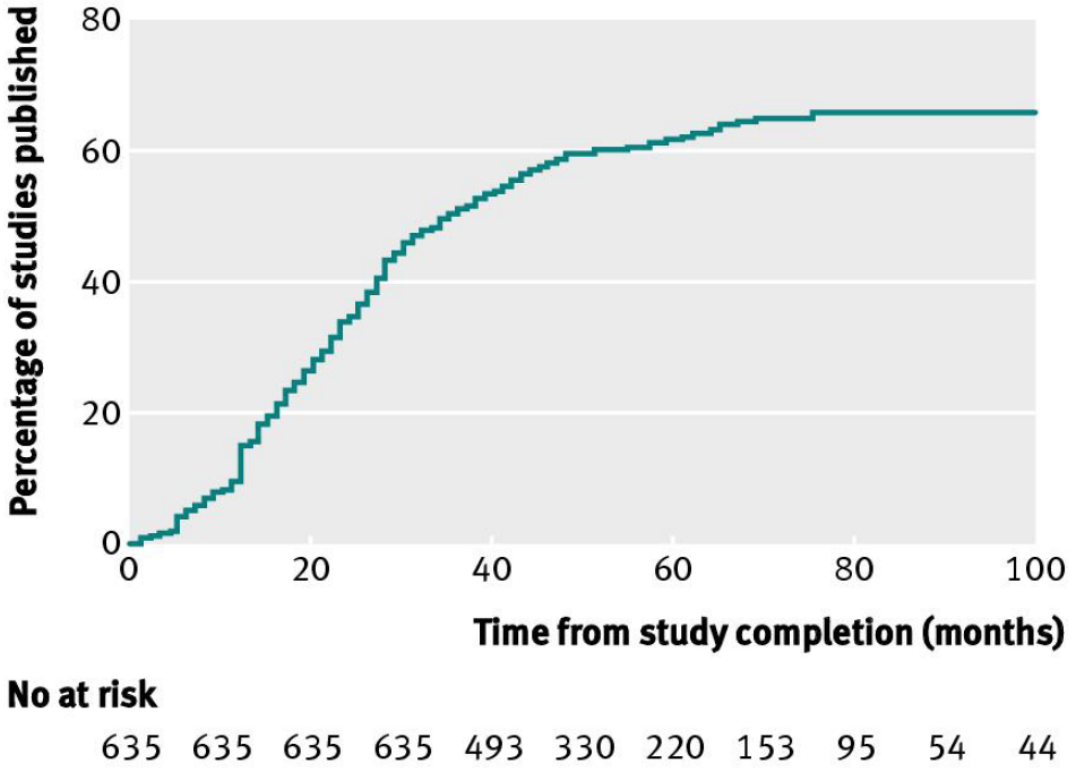
BMJ

BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

RESEARCH

Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis

Joseph S Ross *assistant professor of medicine*[1 2], Tony Tse *program analyst at ClinicalTrials.gov*[3], Deborah A Zarin *director of ClinicalTrials.gov*[3], Hui Xu *postgraduate house staff trainee*[4], Lei Zhou *postgraduate house staff trainee*[4], Harlan M Krumholz *Harold H Hines Jr professor of medicine and professor of investigative medicine and of public health*[2 5 6]



"There are many [NIH-funded] trials not covered by [FDAAA], such as trials of behavioral interventions and surgical procedures. **No policies exist** to make sure that the public has access to results from NIH funded research that is not published"

BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

Purpose of Reforms & Policy Changes

In 2016, NIH announced initiatives targeted to enhance and improve:

Efficiency

Enhance the efficiency of how research studies involving human participants are conducted

Transparency

Promote a culture of transparency in research in order to advance public health

Accountability

Ensure that NIH can appropriately identify and report on their clinical trials portfolio to ensure proper stewardship

Timely Reporting

Decrease the time it takes investigators to publicly report study results

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TOP 10 NIH POLICY CHANGES TO ENHANCE STEWARDSHIP

POLICIES RELEVANT TO *ALL* RESEARCH INVOLVING HUMAN PARTICIPANTS

Single IRB
January 25, 2018

New Application Forms
January 25, 2018

- ✓ Use of a single Institutional Review Board (IRB) for multi-site studies
- ✓ New forms to collect human subjects information
- ✓ Certificates of confidentiality for all research that uses identifiable, sensitive information
- ✓ Expands the Inclusion of Children as Participants in Clinical Research Policy to include individuals of all ages, including older adults

Certificate of Confidentiality
January 25, 2018

Inclusion across the Life Span
January 25, 2019

Single IRB
January 25, 2018

SINGLE INSTITUTIONAL REVIEW BOARD (sIRB)

NOT-OD-16-094: All domestic multi-site studies will use sIRB for ethical review required of non-exempt humans subjects research protocols

Must include a plan that describes:

- The use of a sIRB selected to serve as the IRB of record
- How communications between sites and sIRB will be handled

Standardized agreements have been developed that allow institutions to rely on a sIRB

Exceptions: sIRB not applicable for Career Development (K), Research Training (T), or Fellowship (F) grants

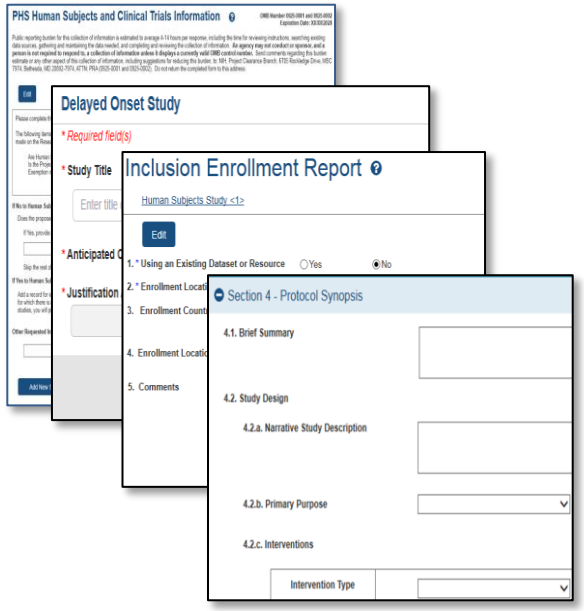
TIP: NCATS SMART IRB platform is a resource for investigators
(SMART: Streamlined, Multisite, Accelerated Resources for Trials)

New Application Forms NOW!

CHANGES TO THE APPLICATION PACKAGE

(NOT-OD-17-062: FORMS-E Application Guide & Package)

PHS Human Subjects and Clinical Trials Information Form



- Collects human subjects, inclusion enrollment, and clinical trial information at the study-level
- Protocol Synopsis, Statistical Plan,
- Includes a Clinical Trials Questionnaire

TIP: Watch the NIH Video that walks through the PHS Human Subjects and Clinical Trials Information Form

ADDITIONAL NIH POLICIES FOR CLINICAL TRIALS

- ✓ Clinical trial-specific Funding Opportunity Announcements (FOAs)
- ✓ New review criteria
- ✓ Expanded registration and results reporting in ClinicalTrials.gov
- ✓ Training in Good Clinical Practice (GCP)

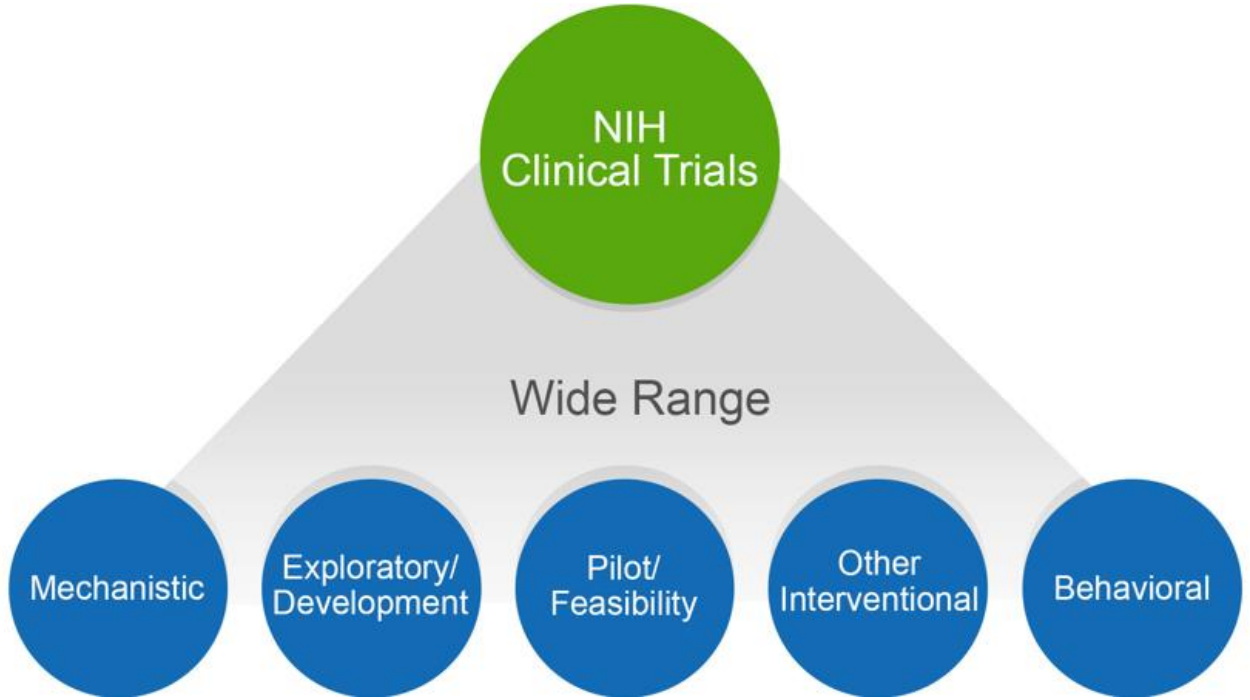
How Does NIH Define a Clinical Trial?

A research study in which one or more **human subjects** are **prospectively assigned** to one or more **interventions** (which may include placebo or other control) to evaluate the effects of those interventions on **health-related biomedical or behavioral outcomes**.

Learn more at https://grants.nih.gov/policy/clinical-trials/definition.htm

NIH Definition of a Clinical Trial is Broad

- Definition was **clarified** and **broadened** in October 2014
- Encompasses a wide range of types of trials, including:
  - Mechanistic
  - Exploratory
  - Pilot/Feasibility
  - Behavioral
- With broader definition, many more studies are classified as clinical trials



New Application Form January 25, 2018

CLINICAL TRIAL QUESTIONNAIRE

Does the study…

1. Involve one or more human subjects?
2. Prospectively assign human subject(s) to one or more intervention(s)?
3. Evaluate the effect of intervention(s) on the human subject(s)?
4. Have a health-related biomedical or behavioral outcome?

If "yes" to ALL – it's a clinical trial

THIS WILL REQUIRE:

- Appropriate FOA Selection
- Writing of research strategy & human subjects sections
- Addressing additional review criteria for clinical trials
- Registering & reporting the trial in ClinicalTrials.gov

Unsure how to answer the questions? We have a tool that can help! https://grants.nih.gov/ct-decision/

Clinical Trial FOAs
January 25, 2018

CLINICAL TRIAL-SPECIFIC FUNDING OPPORTUNITY ANNOUNCEMENTS

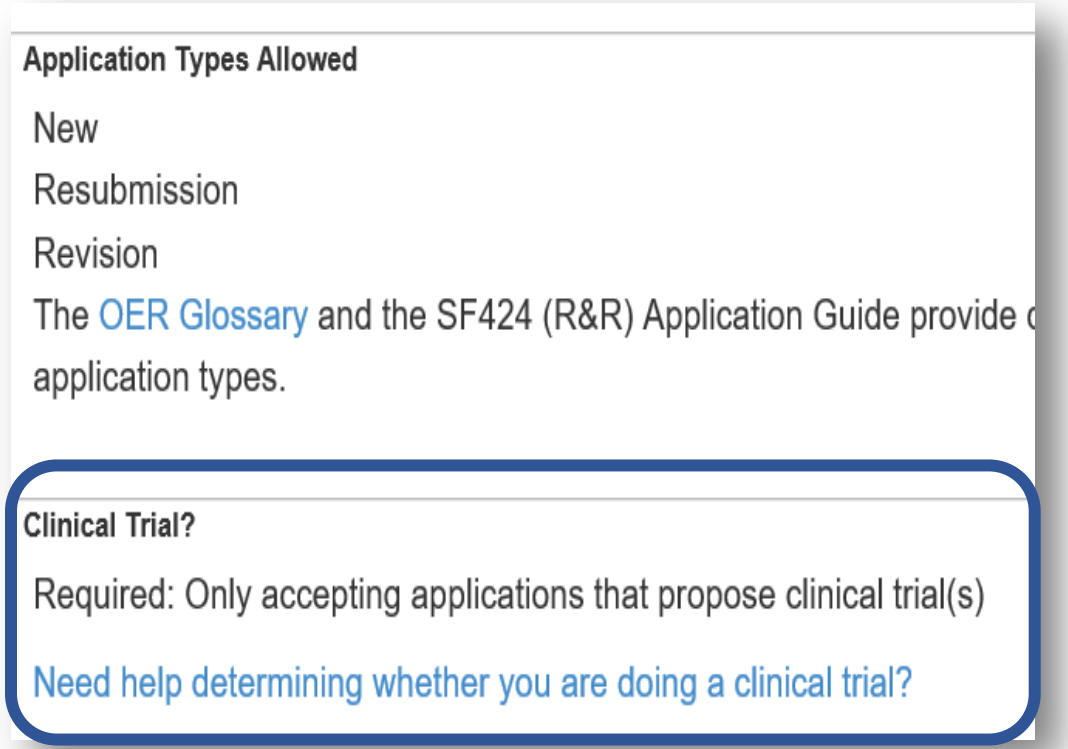
NOT-OD-16-147: All clinical trial applications **MUST** be submitted to an FOA that allows clinical trials

- Clinical Trial - Not Allowed
- Clinical Trial - Optional
- Clinical Trial – Required
- Basic Experimental Studies with Humans (BESH) Required
- Special circumstances for career development awardees – see https://grants.nih.gov/policy/clinical-trials/specific-funding-opportunities.htm

How to Determine if an FOA Accepts Clinical Trials?

FOA Title (new FOAs only)

FOA Section II. Award Information



Tip: Check your FOA at least 30 days before the due date for any updates

NEW NCI CLINICAL TRIAL FUNDING OPPORTUNITIES

NCI DOES NOT PARTICIPATE IN NIH CLINICAL TRIAL-REQUIRED PARENT R01 & R21

PAR-18-560	**DCTD Parent R01- Clinical Trial Required** Investigator-initiated Early Phase Clinical Trials for Cancer Treatment and Diagnosis
PAR-18-559	**DCP-DCCPS Parent R01-Clinical Trial Required** Cancer Prevention and Control Clinical Trials Grant Program

https://www.cancer.gov/grants-training/grants-funding/funding-opportunities

Basic Experimental Studies with Humans (BESH)

Who: Investigators for studies whose primary purpose is the pursuit of basic science and that meet the NIH definition of a "clinical trial" and also the Federal definition of basic science

What: *Delayed Enforcement and Short-Term Flexibilities for Some Requirements Affecting Prospective Basic Science Studies Involving Humans (NOT-OD-18-212)* -- must register and report but can do so through existing basic science portals

When: *Release Date:* July 20, 2018
Effective Through: September 24, 2019

For more information see: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-212.html

Trial Review Criteria
January 25, 2018

REVIEW CRITERIA FOR CLINICAL TRIALS

Clinical Trial FOAs
January 25, 2018

NOT-OD-17-118: FOAs that accept clinical trials will include new review criteria

Scored Review Criteria

- ✓ Significance
- ✓ Investigator
- ✓ Innovation
- ✓ Approach
- ✓ Environment

Additional Review Criteria

- ✓ Study Timeline & Milestones

Read the FOA carefully and be sure your application addresses the review criteria appropriately

Registration
& Reporting
Effective Now!

DISSEMINATION OF NIH-FUNDED CLINICAL TRIAL INFORMATION NOT-OD-16-149

Who: All investigators conducting clinical trials funded in whole or in part by the NIH regardless of trial phase

What: Sponsors need to register* and report results** of trials in ClinicalTrials.gov

Why: Increase the availability of information about clinical trials and their results to the public in a timely manner

*within 21 days of 1st patient enrollment
**no later than 1 year after trial's primary completion date

Good Clinical Practice
Effective Now!

GOOD CLINICAL PRACTICE TRAINING REQUIREMENT

Who: All NIH-funded investigators and NCI staff involved in the *conduct, oversight or management* of clinical trials

What: Both are expected to be trained in GCP consistent with principles of the International Council on Harmonisation

Why: To assure the safety, integrity, and quality of clinical trials

How: Through a class or course, academic training program, or certification from a recognized clinical research professional organization

NOTE: CERTIFICATES SHOULD BE MADE AVAILABLE TO NIH UPON REQUEST

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VISIT THE NIH OFFICE OF EXTRAMURAL RESEARCH FOR DETAILS

https://grants.nih.gov/policy/clinical-trials.htm

Training Resources:
https://grants.nih.gov/policy/clinical-trials/training-resources.htm

- ✓Slides
- ✓Human Subjects/Clinical Trials Questionnaire
- ✓Videos
- ✓Training opportunities

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